Real-World Treatment Switching and Sequencing to Next Line of Therapy of Zanubrutinib, Acalabrutinib, and Ibrutinib in CLL/SLL

Javier Pinilla-Ibarz*[1], Mei Xue[2], Elizabeth Wu[3], Kaitlyn Esselman[3], Wesley Furnback[3], Swetha Challagulla[2], Keri Yang[2]

[1]Moffitt Cancer Center, Tampa, FL, United States of America, *[2]BeiGene USA, Inc., San Mateo, CA, United States of America*, *[3]Real Chemistry, Inc., New York, United States of America*

Background: Evaluating use of Bruton tyrosine kinase inhibitors (BTKis) for the treatment of chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) is crucial to understand real-world outcomes of these therapies in diverse populations.

Aims: The objective of this study was to evaluate real-world switching and sequencing to next line of therapy in patients initiating BTKis as first-line (1L) or second-line (2L) CLL/SLL treatment.

Methods: A retrospective study was conducted using IntegraConnect PrecisionQ to identify adult patients with ≥1 diagnosis for CLL/SLL initiating zanubrutinib, acalabrutinib, or ibrutinib in 1L or 2L between 1/1/2020-2/28/2023 (index period). Index date was defined as date of BTKi initiation. Patients were required to be continuously enrolled for ≥30 days pre- and post-index date. Treatment switching was measured as patients initiating another treatment within same line or advancing to next line of therapy within 90 days. Sequencing to next line of therapy was calculated from time to next treatment Kaplan-Meier curve, censoring patients at end of follow-up, and reported as proportion of patients receiving next line of therapy at 180 days.

Results: 2,816 patients initiated a 1L BTKi (zanubrutinib=157; acalabrutinib=1,238; ibrutinib=1,421) and 1,253 initiated a 2L BTKi (zanubrutinib=107; acalabrutinib=672; ibrutinib=474). No major differences were observed in baseline demographic and clinical characteristics among 1L and 2L BTKi cohorts. Median follow-up in 1L was 123 days for zanubrutinib, 406 days for acalabrutinib, and 637 days for ibrutinib. Regardless of line of therapy, switching rate at ≤60 days and 61-89 days was statistically significantly lower for patients receiving zanubrutinib vs acalabrutinib and ibrutinib ($P<0.0001$, both 1L and 2L) (**Table**). Proportion of patients receiving next line of therapy at 180 days was lower for zanubrutinib vs acalabrutinib and ibrutinib (1L $P=0.2958$; 2L $P<0.0001$) (**Table**).

Summary/Conclusion: Zanubrutinib patients had significantly lower switching rate within 90 days and lower proportion of patients receiving next line of therapy at 180 days when compared with acalabrutinib and ibrutinib in 1L and 2L. Longer follow-up and larger zanubrutinib sample size are required for a comprehensive assessment of treatment outcomes associated with use of BTKis in CLL/SLL.

Table. Treatment switching and proportion of patients receiving next line of therapy for patients initiating BTKis in 1L and 2L

1L	Zanubrutinib (n=157)	Acalabrutinib (n=1238)	Ibrutinib (n=1421)
Switching (%)*			
≤60 days	10.2%	17.1%	13.1%
61-89 days	0.0%	3.4%	2.5%
% of patients receiving next line of therapy at 180 days	13.9%	24.5%	21.1%
2L	**Zanubrutinib** (n=107)	**Acalabrutinib** (n=672)	**Ibrutinib** (n=474)
Switching (%)*			
≤60 days	7.5%	10.7%	17.1%
61-89 days	0.0%	2.5%	4.0%
% of patients receiving next line of therapy at 180 days*	9.1%	18.6%	29.2%

*P<0.0001

1L, first line; 2L, second line; BTKis, Bruton tyrosine kinase inhibitors.